AMENDMENTS TO THE CLAIMS:

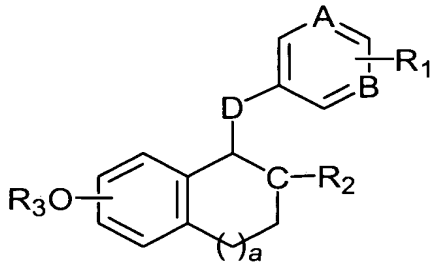
This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of claims

What is claimed is:

1-33. (Canceled)

34. (Presently Amended) A method for modulating ER-β in a cell expressing ER-β, comprising contacting the cell with an effective amount of a compound ~~of claim 1~~ having the structure:



or a pharmaceutically acceptable salt thereof;

wherein

a is 0, 1 or 2;

A, B and C are independently CH, CR or N;

D is $-(CH_2)_r-$ or $-(CH_2)_nC(=O)(CH_2)_m-$;

R_1 represents one or two substituents independently selected from -X-Y;

R_2 is C_{1-8} alkyl, C_{6-12}aryl, C_{7-12}aralkyl, $-C(=O)R_5$, a five- or six-membered heterocycle or heterocyclealkyl containing up to two heteroatoms selected from O, NR_c and $S(O)_q$, or a bicyclic ring system contain a five- or six-membered heterocycle fused to phenyl, wherein each of the above groups are optionally substituted with one to three substituents independently selected from -X-Y or R_4; and

R_3 is hydrogen,$-R_6$, $-(CH_2)_sC(=O)R_6$, $-(CH_2)_sC(=O)OR_6$, $-(CH_2)_sC(=O)NR_6R_7$, $-(CH_2)_sC(=O)NR_6(CH_2)_nC(=O)R_7R_8$, $-(CH_2)_sNR_6C(=O)R_7$, $-(CH_2)_sNR_6C(=O)NR_7R_8$, $-(CH_2)_sNR_6R_7$, $-(CH_2)_sOR_6$, $-(CH_2)_sSO_qR_6$ or $-(CH_2)_sSO_2NR_6R_7$;

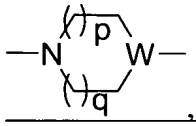
and wherein

R_4 is at each occurrence independently halogen, hydroxy, carboxy, C_{1-6}alkyl, C_{1-4}alkoxy, C_{1-4}haloalkyl, acyloxy, C_{1-4}thio, C_{1-4}alkylsulfinyl, C_{1-4}alkylsulfonyl, (hydroxy)C_{1-4}alkyl, C_{6-12}aryl, C_{7-12}aralkyl, -C(=O)OH, -C(=O)OR, -OC(=O)R, -C(=O)NHR, -C(=O)NRR, -C(=O)NHOR, $-SO_2NHR$, $-NHSO_2R$, -CN, $-NO_2$, C_{1-4}alkylamino, C_{1-4}dialkylamino, -NHC(=O)R, $NHC(=O)(CH_2)_s$(five- or six-membered heterocycle), a five- or six-membered heterocycle, or a five-or six-membered heterocycle fused to phenyl;

R_5, R_6, R_7 and R_8 are at each occurrence independently hydrogen, C_{1-8}alkyl, C_{6-12}aryl, C_{7-12}aralkyl, or a five- or six-membered heterocycle or heterocyclealkyl containing up to two heteroatoms selected from 0, NR_c and $S(O)_q$, wherein each of the above groups are optionally substituted with one to three substituents independently selected from R_4;

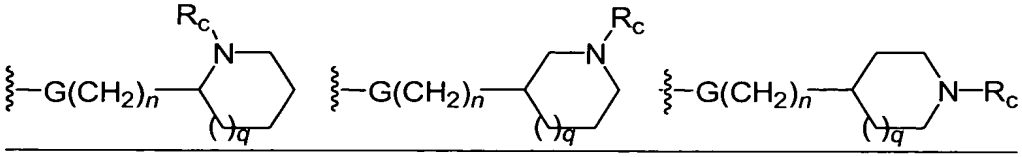
X is at each occurrence independently a direct bond; $-(CH_2)_nZ(CH_2)_m-$; $-O(CH_2)_nZ(CH_2)_m-$; $-S(CH_2)_nZ(CH_2)_m-$; $-NR_c(CH_2)_nZ(CH_2)_m-$; $-O(CH_2)_nCR_aR_b-$; $-NR_c(CH_2)_nCR_aR_b-$; $-OCHR_cCHR_d-$; or $-SCHR_cCHR_d-$;

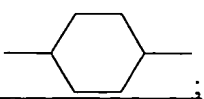
Y is at each occurrence independently halogen; $-R_e$; $-NR_eR_f$;



, optionally fused on adjacent carbon atoms with one or two phenyl or cycloalkyl rings, and with each carbon optionally and independently substituted with carbonyl or with one or two substituents independently selected from R_4, with any two R_4 substituents on a single carbon atom optionally being taken together to form a five- or six-membered heterocycle, and with each nitrogen atom optionally and independently substituted with R_4, wherein W is $-NR_e-$, -O-, -S- or $-CR_eR_f-$; or a bridged or fused C_{5-12}bicyclic amine optionally substituted with one to three substituents independently selected from R_4;

or where -X-Y is



Z is CH_2, CH=CH, C≡C, O, NR_c, $S(O)_q$, C(=O), $C(OH)R_c$, $C(=O)NR_c$, $NR_cC(=O)$, $C(=O)NR_c$, $NR_cC(=O)$ or  ;

G is O, S or NR_e;

n and *m* are at each occurrence independently 0, 1, 2 or 3;

p is at each occurrence independently 1, 2 or 3;

q is at each occurrence independently 0, 1 or 2;

r is at each occurrence independently 1, 2, 3, 4 or 5;

s is at each occurrence independently 0, 1, 2, 3 or 4;

R is at each occurrence independently C_{1-6}alkyl;

R_a and R_b are at each occurrence independently C_{1-8}alkyl or taken together form a C_{3-8}cyclic alkyl;

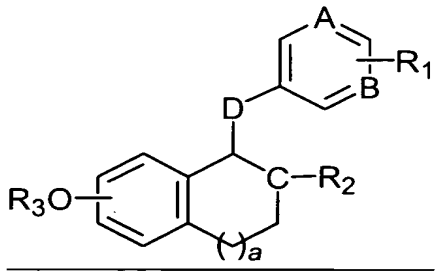
R_c and R_d are at each occurrence independently hydrogen or C_{1-4}alkyl; and

R_e and R_f are at each occurrence independently hydrogen, C_{6-12}aryl, C_{1-8}alkyl, C_{7-12}aralkyl, a five- or six-membered heterocycle, or a five- or six membered heterocycle fused to phenyl; or wherein R_e or R_f form a 3-8 membered nitrogen-containing heterocyclic alkyl with R_a or R_b; and wherein each R_e and R_f are optionally substituted with up to three substituents independently selected from R_4.

35. (Presently Amended) The method of claim ~~32~~ 34 wherein the cell preferentially expresses ER-β over ER-α.

36. (Original) The method of claim 35 wherein the cell is bone, bladder, uterus, ovary, prostate, testis, epididymis, gastrointestinal tract, kidney, breast, eye, heart, vessel wall, immune system, lung, pituitary, hippocampus or hypothalamus cell.

37. (Presently Amended) A method for modulating ER-β in tissue expressing ER-β, comprising contacting the tissue with an effective amount of a compound ~~of claim 1~~ having the structure:



or a pharmaceutically acceptable salt thereof;

wherein

a is 0, 1 or 2;

A, B and C are independently CH, CR or N;

D is $-(CH_2)_r-$ or $-(CH_2)_nC(=O)(CH_2)_m-$;

R_1 represents one or two substituents independently selected from -X-Y;

R_2 is C_{1-8} alkyl, C_{6-12}aryl, C_{7-12}aralkyl, $-C(=O)R_5$, a five- or six-membered heterocycle or heterocyclealkyl containing up to two heteroatoms selected from O, NR_c and $S(O)_q$, or a bicyclic ring system contain a five- or six-membered heterocycle fused to phenyl, wherein each of the above groups are optionally substituted with one to three substituents independently selected from -X-Y or R_4; and

R_3 is hydrogen, $-R_6$, $-(CH_2)_sC(=O)R_6$, $-(CH_2)_sC(=O)OR_6$, $-(CH_2)_sC(=O)NR_6R_7$, $-(CH_2)_sC(=O)NR_6(CH_2)_nC(=O)R_7R_8$, $-(CH_2)_sNR_6C(=O)R_7$, $-(CH_2)_sNR_6C(=O)NR_7R_8$, $-(CH_2)_sNR_6R_7$, $-(CH_2)_sOR_6$, $-(CH_2)_sSO_qR_6$ or $-(CH_2)_sSO_2NR_6R_7$;

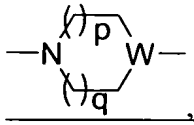
and wherein

R_4 is at each occurrence independently halogen, hydroxy, carboxy, C_{1-6}alkyl, C_{1-4}alkoxy, C_{1-4}haloalkyl, acyloxy, C_{1-4}thio, C_{1-4}alkylsulfinyl, C_{1-4}alkylsulfonyl, (hydroxy)C_{1-4}alkyl, C_{6-12}aryl, C_{7-12}aralkyl, -C(=O)OH, -C(=O)OR, -OC(=O)R, -C(=O)NHR, -C(=O)NRR, -C(=O)NHOR, $-SO_2NHR$, $-NHSO_2R$, -CN, $-NO_2$, C_{1-4}alkylamino, C_{1-4}dialkylamino, -NHC(=O)R, $NHC(=O)(CH_2)_s$(five- or six-membered heterocycle), a five- or six-membered heterocycle, or a five-or six-membered heterocycle fused to phenyl;

R_5, R_6, R_7 and R_8 are at each occurrence independently hydrogen, C_{1-8}alkyl, C_{6-12}aryl, C_{7-12}aralkyl, or a five- or six-membered heterocycle or heterocyclealkyl containing up to two heteroatoms selected from 0, NR_c and $S(O)_q$, wherein each of the above groups are optionally substituted with one to three substituents independently selected from R_4;

X is at each occurrence independently a direct bond; $-(CH_2)_nZ(CH_2)_m-$; $-O(CH_2)_nZ(CH_2)_m-$; $-S(CH_2)_nZ(CH_2)_m-$; $-NR_c(CH_2)_nZ(CH_2)_m-$; $-O(CH_2)_nCR_aR_b-$; $-NR_c(CH_2)_nCR_aR_b-$; $-OCHR_cCHR_d-$; or $-SCHR_cCHR_d-$;

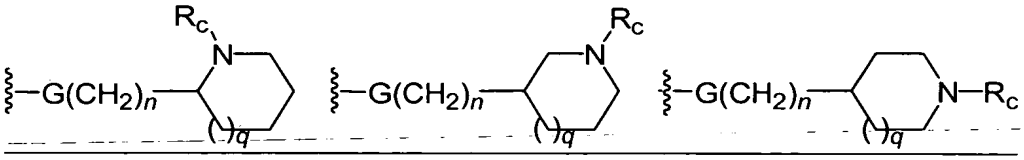
Y is at each occurrence independently halogen; $-R_e$; $-NR_eR_f$;

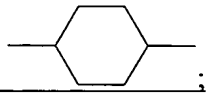


, optionally fused on adjacent carbon atoms with one or two phenyl or cycloalkyl rings, and with each carbon optionally and independently substituted with

carbonyl or with one or two substituents independently selected from R_4, with any two R_4 substituents on a single carbon atom optionally being taken together to form a five- or six-membered heterocycle, and with each nitrogen atom optionally and independently substituted with R_4, wherein W is $-NR_e-$, -O-, -S- or $-CR_eR_f-$; or a bridged or fused C_{5-12}bicyclic amine optionally substituted with one to three substituents independently selected from R_4;

or where -X-Y is



Z is CH_2, CH=CH, C≡C, O, NR_c, $S(O)_q$, C(=O), $C(OH)R_c$, $C(=O)NR_c$, $NR_cC(=O)$, $C(=O)NR_c$, $NR_cC(=O)$ or  ;

G is O, S or NR_e;

n and *m* are at each occurrence independently 0, 1, 2 or 3;

p is at each occurrence independently 1, 2 or 3;

q is at each occurrence independently 0, 1 or 2;

r is at each occurrence independently 1, 2, 3, 4 or 5;

s is at each occurrence independently 0, 1, 2, 3 or 4;

R is at each occurrence independently C_{1-6}alkyl;

R_a and R_b are at each occurrence independently C_{1-8}alkyl or taken together form a C_{3-8}cyclic alkyl;

R_c and R_d are at each occurrence independently hydrogen or C_{1-4}alkyl; and

R_e and R_f are at each occurrence independently hydrogen, C_{6-12}aryl, C_{1-8}alkyl, C_{7-12}aralkyl, a five- or six-membered heterocycle, or a five- or six membered heterocycle fused to phenyl; or wherein R_e or R_f form a 3-8 membered nitrogen-containing heterocyclic alkyl with R_a or R_b; and wherein each R_e and R_f are optionally substituted with up to three substituents independently selected from R_4.

38. (Original) The method of claim 37 wherein the tissue preferentially expresses ER-β over ER-α.

39. (Original) The method of claim 38 wherein the tissue is tissue of bone, bladder, uterus, ovary, prostate, testis, epididymis, gastrointestinal (GI) tract, kidney, breast, eye, heart, vessel wall, immune system, lung, pituitary, hippocampus or hypothalamus.

40-45. (Canceled)